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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,199	05/31/2001	Jean-Charles Schwartz	P06853US00/L	8229

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EXAMINER	
SEAMAN, D MARGARET M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 09/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,199	SCHWARTZ ET AL.	
	Examiner	Art Unit	
	D. Margaret Seaman	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-96,98-122,124,128 and 154-156* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-96,98-122,124,128 and 154-156* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application was filed 5/31/2001 and is a 371 of PCT/EP99/05744 (7/29/1999) which claims priority to EP 98401944.8 (7/29/1998) and EP 98403351.4 (12/31/1998). Claim 97 has been canceled. Claims 89-96, 98-122, 124, 128, and 154-156 are before the Examiner.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 89-96, 98-121, 124, 128, and 154-156 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the scope of enablement requirement, is upheld. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The only compound to which has been connected to the treatment of Alzheimer disease, attention, wakefulness or memorization disorder is the compound of example 117 (page 121) of the instant specification which is 3-(4-chlorophenyl)propyl-3-piperidinopropyl ether by the affidavit of 6/4/2004. All other compounds are not seen to be enabling for the instant methods.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims,
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The nature of the invention is the method of treating Alzheimer's disease, attention, wakefulness and/or memorization disorder by using a compound that inhibits H3-receptor.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence

of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. Applicant states on page 2 of the affidavit (paragraph 6.2) that the effects of the H3 receptor antagonists have not yet been studied in persons with attention, wakefulness and memory disorders or Alzheimer's disease.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of all diseases, whether or not the modulation of histamine H3-receptors would make a difference in the disease. Hence, in the absence of a showing of a nexus between attention, wakefulness and memory disorders or Alzheimer's disease and the modulation of histamine H3 receptors, one of ordinary skill in the art is unable to fully predict possible results from the administration of the method of claim 89 due to the unpredictability of the role of modulation of histamine H3 receptors.

The presence or absence of working examples: The specification and subsequent declarations have data that shows that some of the instant Markush of compounds do act as histamine He antagonists. In the affidavit of 6/4/2004, only one compound

(example 117) has been tested and shows promise. However, this does not enable the full scope of the compounds encompassed by the instant claims.

Further, the affidavits presented in March 2005 disclose many different variations of chain A", X" and chain B". However, this does not cover the many and varied moieties covered by Y" or NR^1R_2. These can be many varied and different things. This variety has not been covered sufficiently by the instant specification or the affidavits presented to date.

The amount of direction or guidance present: The guidance present in the specification is that of the compounds that are tested for H3 inhibition and that some work, some don't work, and some work to a weak extent. Very similar compounds have been shown to have one inhibit H3 well and the other have no effect. Page one of the specification states that histamine He receptors are thought to play an important role in a variety of inflammatory diseases and CNS disorders. The specification does not seem to enable a correlation between the mediation of histamine H3 receptors and the treatment of any and all diseases. Applicant stated in the affidavit that H3 receptor antagonists have not yet been studied in persons with the instant conditions.

The breadth of the claims: The claims are drawn to the treatment of Alzheimer's disease, attention, wakefulness and/or memorization disorders mediated by the histamine H3 receptor.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine what compounds out of all the

millions of compounds encompassed by the instant claim 89 can treat the instantly claimed disorders that are mediation by histamine H3 receptors and then would further need to determine which of the claimed compounds would provide treatment of the claimed disorders/disease.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds encompassed by the instant method claim 89 for the treatment of Alzheimer's disease, attention disorder, wakefulness disorder or memorization disorder. As a result necessitating one of ordinary skill to perform an exhaustive search for which compounds can be used in the instant method claim 89 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success.

Further, the affidavits presented in March 2005 disclose many different variations of chain A" and chain B". However, this does not cover the many and varied moieties covered by Y" or NR1R2. These can be many varied and different things. This variety has not been covered sufficiently by the instant specification or the affidavits presented to date. The affidavits/documents presented cover the instant variety of ChainA", X" and chain B". However, NR^1R_2 and Y" are not fully enabled by the instant specification. Due to this, the rejection stands.

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 89-96, 98-122, 124, 128, and 154-156 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, claims 89 and 117 are ambiguous due to the claims being drawn to "other aldehyde derivatives" and "other ketone derivatives" among others. Such language is not limited and has no definition within the specification. Due to this, the claims are ambiguous.

Claim 124 is ambiguous due to the claim limiting ""the heterocycle" to containing a S atom. However, it is unclear as to what or which heterocycle is being referred to.

Claim 156 is ambiguous due to the claim limiting the cognitive disorder of claim 89 to Alzheimer's disease. However, claim 89 is limited to "cognitive disorders selected from the group consisting of attention, wakefulness and memory disorders". There is no Alzheimer's disease in claim 89.

Claims 89-96, 98-122, 124, 128, and 154-156 are ambiguous to as being drawn to polymorphic crystalline structures. However, specific polymorphic crystalline structures are not predictable. They vary from compound to compound and from hydrate to hydrate and from different salt to salt. Due to this, all polymorphic crystalline structures is ambiguous.

Claims 89-96, 98-12, 124, 128, and 154-156 are ambiguous due to the claims being drawn to "as a ligand of the histamine H3-receptors". What does this mean? Clarification is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. Margaret Seaman whose telephone number is 571-272-0694. The examiner can normally be reached on 630am-4pm, First Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecelia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. Margaret Seaman
Primary Examiner
Art Unit 1625

dms